

A challenge to research

David Spurgeon

Current contraceptive technology cannot be regarded as adequate to meet either individual or societal needs in either industrial or developing nations, and funding must be continued at a much higher level in order to improve it.

That is the conclusion of a study involving more than 160 experts in 26 nations that was initiated by the Ford Foundation, with the collaboration of the Rockefeller Foundation and the IDRC. The study has resulted in a report, *Reproduction and Human Welfare: A Challenge to Research*, (Roy O. Greep, Marjorie A. Koblinsky, and Frederick S. Jaffe, published by the MIT Press).

A decline in funding for contraceptive research led to the study: in the face of growing worldwide population problems, funding dropped after reaching a peak in 1974 of \$119 million, to less than \$109 million in 1976. The report concludes that at least three times the 1974 level (or about \$361 million) is needed to pursue research leads for new, effective, reversible, safe and inexpensive fertility control methods.

Those responsible for the study do not expect to find an ideal, all-purpose contraceptive suitable for every individual. The diversity of personal, cultural, religious and economic circumstances is too great – and in fact the needs of the individual vary at different stages of life.

"What is needed," says the book, "is a broad array of contraceptive methods that require less complex distribution systems, that are safer, less discomfiting, and more convenient than current methods, that combine high acceptability with high continuity of use, and that are suited to the diverse requirements of the world."

In discussing the book (which he says gathers and orders "what we know and do not know about the reproductive process"), McGeorge Bundy, president of the Ford Foundation, told a press conference that while "some of us may have become rather inured to cries of alarm about the 'population explosion'... the fact remains that the growth of human population in the developing world continues at unprecedented levels."

"While fertility has begun to fall in six of the eight largest developing countries, so has mortality, and the next quarter century is expected to witness a continuation of the very high rate of population growth – about 2.3 percent per annum – experienced in the last 25 years."

Whether population grows exponentially in the 21st Century, or whether as projected by the United Nations, the rate of growth starts decreasing, to stabilize sometime after 2075, the consequences for human welfare are deeply disturbing, McBundy said. Illiteracy will increase as the number of children surpasses the expansion of school facilities, unemployment will increase, income will be even more unevenly distributed, and the population will be fed only if large areas of currently unexploited land are brought under cultivation.

But population problems are not confined to the developing world, said Bundy. "While population growth in the United States has ceased to be a problem that alarms us at the moment, the epidemic of unplanned, illegitimate adolescent

pregnancies is a grave domestic problem." Fifty-four percent of all births to teenagers in the United States in 1974 were conceived out of wedlock and about two-thirds of these babies were born out of wedlock. In addition, one third of abortions performed in the United States are on teenagers.

Currently used contraceptive methods are in general quite safe – and certainly, for women up to the age of 40, safer than the risks associated with pregnancy. For example, Dr. Kenneth J. Ryan, chairman of Harvard Medical School's department of obstetrics and gynaecology, said: "The maternal mortality rate for pregnancy is 20 per 100,000 in developed nations and averages 40 per 100,000 where medical care is less advanced. The mortality rate for the pill user is 3 per 100,000..."

The contraceptive pill is also the most effective method of birth control. In fact, Dr. Ryan said, there is an inverse relationship between success of a contraceptive method in preventing pregnancy and the safety of the method used. But the lower safety of the most effective methods is compensated for by removal of the risk inherent in the extra pregnancies they prevent.

Thus the risk of death for women taking the pill is five-fold lower than that for women who use no contraceptives and risk pregnancy instead. The so-called "safer" methods, such as the diaphragm or the condom, may on balance be more dangerous than oral contraceptives to the extent that they are less effective in preventing pregnancy.

Despite this, current methods of contraception still have many drawbacks. Pill users do risk side effects, ranging from benign liver tumours, myocardial infarction (heart attack), and ectopic pregnancy (one that occurs outside the womb), to gall bladder disease. The side effects may even include malignancies of the uterus and the breast, though to date this has not been proved. "Since it is well known that the development of a malignancy may take many years, this issue cannot be regarded as settled," said Dr. Elizabeth B. Connell, associate director for health sciences at the Rockefeller Foundation.

Dr. Connell went on to list side effects of the intra-uterine devices (IUDs), including perforation of the uterus at time of insertion, development of pain and bleeding necessitating removal, and increased risk of spontaneous abortion with the Dalkon shield (a variety of IUD) when it was left in place after pregnancy occurred. Infections were increased almost seven-fold with almost all IUDs, sometimes making future childbearing impossible, Dr. Connell said, suggesting to some that women who had never had children should not perhaps use them. And as with the pill, there is increased risk of ectopic pregnancy.

All these risks, reported in the press, have led in recent months to an increasing number of women returning to safer but less effective methods of contraception, Dr. Connell said.

The authors of *Reproduction and Human Welfare* and the experts assembled at the Ford Foundation news briefing discussed a number of promising avenues of research to develop alternatives to current contraceptives. These included an anti-pregnancy vaccine (see page 12); a pill for

males to suppress sperm formation; drugs that keep the fertilized ovum from implanting in the womb; longer-acting contraceptive agents that can be given by injection, implanted under the skin or absorbed through an inter-vaginal ring; and a substance that, when administered to a young male, would allow him to develop normally sexually but would block sperm production until he was ready to become a father.

The male pill of the future probably will contain the male sex hormone, testosterone. It will have to be taken with absolute regularity, because sperm reproduction would begin immediately the user stopped taking it. Tests already have been carried out with such a pill.

The proposed contraceptive for the young sexually active male who is not ready to become a father is so far just hypothetical, but it is theoretically feasible. The proposal follows on the very recent discovery of a substance that may be a hormone, produced by the Sertoli cells in the testes. The substance has been named inhibin because it inhibits another hormone, FSH, believed to be necessary for formation of spermatozoa. If this substance could be administered orally or otherwise, it could prevent sperm formation until fatherhood was desired.

Current female oral contraceptives use a high dose of estrogen to block ovulation — and it is this that causes the side effects. Another way to prevent pregnancy would be to block the action of the hormone progesterone, which is absolutely necessary to prepare the uterus for the implantation of the fertilized egg. This method would avoid overdosing the woman with a hormone and thus upsetting her metabolism. A contraceptive that would block the action of progesterone (which is required for little else than conception and maintenance of pregnancy) is believed to be possible given adequate funds.

Four long-acting injectable contraceptives for women are already being used in various countries (they are effective from one to three months). They are well received because women in developing countries (and some in the United States) believe injectable drugs are more effective and they are used to receiving them. The drugs are also easily administered by relatively untrained personnel. Research is necessary to remove the major side effect — abnormal bleeding and cessation of menstruation. Clinical trials have also been undertaken on steroids inserted under the skin, which could be effective from six months to six years. And a vaginal ring has been tested that contains a contraceptive steroid that is absorbed through the vagina. The ring is fitted by the wearer and can be used for six months.

To develop such methods — and possibly others — the authors of *Reproduction and Human Welfare* say about \$500 million will be needed by 1980. And the bulk of the funds will have to come from governmental agencies, principally in the United States, Europe, Canada, Israel, Australia and Japan, and the international assistance agencies. □

Science writer David Spurgeon is director of the IDRC's Publications Division, and editor of Science Forum.

Birth control methods of the future may include a nasal spray now undergoing trials in four countries. The spray works by depressing the centre in the brain that releases hormones necessary for pregnancy, says its developer, Dr. T.C. Anand Kumar, of the Department of Anatomy of the All-India Institute of Medical Science.

His experiments were described with several others on the frontier of birth control research at a recent seminar organized by the Zoology Department of Delhi University.

The active ingredient of Dr. Kumar's spray is a minute dose of progesterone, the female hormone used in birth control pills. The two-microgram dose is sprayed up the nostril six to 10 days after the menstrual cycle begins. No side effects were found in extensive experiments on monkeys, Dr. Kumar said.

His institute recommended the spray to an international organization which is now testing it at two centres in India, three in Korea, in Mexico and in London, England. Dr. Kumar says the spray needs at least two years more testing in experimental field trials.

Dr. M. R. Prasad, of Delhi University's Zoology Department, gave a German-produced drug called cyproterone acetate to male lab animals. He found sperm cells did not mature as a result. Sperm production was not reduced, but normal animal mating resulted in no pregnancies. The World Health Organization (WHO) took up Dr. Prasad's animal results and arranged for clinical tests in Germany and at India's National Institute of Health and Family Planning (NIHFP).

Dr. N.R. Moudgal, a biochemistry professor at Bangalore's Indian Institute of Science, used an injected animal antibody to neutralize the hormone released from the fertilized egg that keeps the fetus-to-be attached to the wall of the uterus. With this hormone neutralized, monkeys which were injected in the first month of their missed period, had normal menstruation three days after injection. The process now awaits clearance from the All-India Institute of Medical Science, for human experimentation to neutralize the human hormone, chorionic gonadotrophin.

Another All-India researcher, Dr. K.R. Laumas, has had 100 percent success with reversing sterilization in rats. In vasectomy the sperm-carrying tubes are cut, making the sterilization permanent. Instead, Dr. Laumas inserts a thread-like copper-alloy wire into the tube. This blocks sperm and sterilizes the rat. To reverse sterilization, the wire is simply removed in another operation. Dr. Laumas is continuing the experiments in monkeys.

India's Central Drug Research Institute has developed a new drug called centchroman, believed to have potential as a post-coital ("morning after") contraceptive. It has worked on several kinds of laboratory animals, and may now be tried on humans, the seminar was told.

Meanwhile, a recent report from the NIHFP cautions, "Although some effective methods for contraception are available, none can be said to be free from some drawbacks, either in the form of side effects and/or in lacking ease and simplicity of use. A large number of people are taking chemical and biological preparations as a result of modern medical public health and family planning practices. There are wide gaps in our knowledge in these fields, particularly in that pertaining to the human being."

The report points out that birth control is evolving into family planning, and will become family welfare planning, making the scientific objective much wider than mere family limitation.

The objective is now extended, the report says, to include total family welfare, including spacing and limitation of children, treatment of the infertile, mother and child care, and ultimately an improvement in the quality of the population.

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